Quantifying physiology-ecology feedback enables prediction of microbial community dynamics

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***Short Abstract* — Predicting microbial community dynamics is critical for controlling communities. It should be trivial to predict the growth rate of a simplified community of two cross-feeding *S. cerevisiae* strains. However, a model based on parameters measured from batch cultures matches experiments poorly despite its previous success in predicting for example steady-state strain ratio. Here, we find that metabolite release rate can vary significantly with growth rate. Thus, we need to consider how physiology (e.g. growth rate) impacts ecology (e.g. metabolite release rate) in addition to how ecology affects physiology. Incorporating this ecology-physiology feedback enables prediction of community dynamics.**

***Keywords* — Microbial community dynamics; Microbial physiology and ecology**

I. Purpose

Microbial communities are ubiquitous, and impact us and our ecosystems. Commensal gut microbiota influence our body weight and immune system [1]. Microbial communities are also used in pollutant degradation [2] and in industrial production of important compounds [3]. To control microbial communities, we need to understand how interactions between species lead to community dynamics.

Here, we attempt to predict the growth rate of an engineered yeast community CoSMO (Cooperation that is Synthetic and Mutually Obligatory") [4]. CoSMO comprises two differentially-fluorescent non-mating haploid strains. The A^-L^+ strain requires adenine due to deletion of *ADE8*, and over-activates the lysine biosynthetic pathway due to a feedback-resistant *LYS21* mutation. The L^-A^+ strain requires lysine due to deletion of *LYS2*, and over-activates the adenine biosynthetic pathway due to a feedback-resistant *ADE4* mutation. Overproduced metabolites are released into the environment. In minimal medium lacking adenine and lysine supplements, the two strains engage in obligatory cooperation.

In a well-mixed environment, CoSMO dynamics can be modeled by ordinary differential equations. In our earlier study on CoSMO [4], we quantified some of the model parameters and "borrowed" others from the literature. Model parameters correspond to strain phenotypes such as metabolite release rate, metabolite consumption per new cell, death rate, and birth rates at various concentrations of the required metabolite. Our model correctly predicted, for example, the steady state strain ratio [4] and qualitative features of community spatial organization [5]. However, predictions on steady state CoSMO growth rate poorly matched experiments.

Here, we re-measure each strain's phenotypes in chemostat cultures where growth rates are set at various levels that span the steady state CoSMO growth rate. We find that both populations rapid evolve during measurements, and we devise methods to mitigate the effects of rapid evolution.

We find that within the range of environments that CoSMO experiences, lysine release rate of A^-L^+ varies significantly with growth rate. Thus, besides modeling how ecological interactions affect cell physiology (growth rate), we need to consider how cell physiology (growth rate) affects ecological interactions (release rates). When we incorporate growth rate-dependent release rate (physiology-ecology feedback), our model agrees with experimental results.

II. Conclusion

Quantitative prediction of microbial community dynamics may require quantifying physiology-ecology feedback. When model parameters are measured (instead of "borrowed"), model-experiment discrepancy motivates new discoveries.

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